

TOBACCO SMOKING

First listed in the *Ninth Report on Carcinogens*

CARCINOGENICITY

Tobacco smoking is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans which indicate a causal relationship between tobacco smoking and human cancer (reviewed in IARC V.38, 1986; Burns et al., 1997a).

Tobacco smoking has been determined to cause cancer of the lung, urinary bladder, renal pelvis, oral cavity, pharynx, larynx, esophagus, lip, and pancreas in humans. Lung cancer deaths are associated with certain tobacco smoking patterns, increasing with increasing consumption of tobacco products and decreasing in certain groups as the amount smoked declines. Smoking cessation is associated with a decreased risk of developing cancer. The carcinogenic effects of tobacco smoke are increased in individuals with certain predisposing genetic polymorphisms.

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Tobacco smoke has been demonstrated to be carcinogenic in several species of experimental animals. The evidence is most clearly established for the larynx in the hamster following inhalation of tobacco smoke, and for the skin of mice receiving dermal applications of tobacco smoke condensates. Tumors of the respiratory tract have also been reported in rats exposed to cigarette smoke. Individual chemical components of tobacco smoke have been shown to be carcinogenic to humans and/or experimental animals. Tobacco smoke or tobacco smoke condensates cause cell transformation and mutations or other genetic alterations in a variety of *in vitro* and *in vivo* assays. The urine of smokers has been found to be mutagenic and there is evidence of more chromosomal damage in the somatic cells of smokers than in nonsmokers.

PROPERTIES

Nearly 4000 chemicals have been found in tobacco smoke (Vineis and Caporaso, 1995; Hoffmann and Hoffmann, 1995; IARC V.38, 1986), including acrolein, aromatic amines, benzene, formaldehyde, nitrosamines, polycyclic aromatic hydrocarbons, urethan (ethyl carbonate), radioactive elements (radium-226, radium-228, thorium-228, polonium-210), arsenic, nickel, chromium, and cadmium.

USE

Currently, the primary source for tobacco smoking is cigarettes, the others being the use of pipes and cigars. The use of pipes and cigars was more prevalent in the 18th and 19th centuries, but there was a shift from these products to cigarettes after 1910, following mass marketing campaigns for cigarettes (IARC V.38, 1986; Burns et al., 1997a). Per capita consumption of cigarettes in the United States rose from 54 in 1900 (U.S. DHHS, 1989; cited by Burns et al., 1997a,b) to a peak of 4,345 in 1963 (Burns et al., 1997b).

The use of tobacco products varies among racial, gender, and age groups. Currently,

males have a higher prevalence of smoking than females (U.S. DHHS, 1980; cited by Burns et al., 1997b). Advertising campaigns began targeting the male population many years before targeting females, which may explain why men began smoking earlier in the century than women (U.S. DHHS, 1980; cited by Burns et al., 1997b). Smoking prevalence and cessation also vary with educational attainment (U.S. DHHS, 1989; Pierce et al., 1989; both cited by Burns et al., 1997b).

PRODUCTION

Tobacco has been an important economic agricultural crop since the 1600s. North and Central America produced the highest quantity, with 1,158,506 tons harvested in 1982 (IARC V.38, 1986). *Nicotiana tabacum* is the most common species of tobacco used in cigarettes, but *N. rustica* is also used in some areas (Garner, 1951; Wynder and Hoffmann, 1963; Tso, 1972; Akehurst, 1981; all cited by IARC V.38, 1986). For smoking tobacco, the tobacco leaf material is manipulated by physical and chemical methods during the manufacturing process, some of which are intended to reduce the yields of toxic agents and tars in smoke. The tobacco is fine cut and wrapped in paper for consumption. Generally, cigarettes are a blend of different flue-cured grades, burley, Maryland, and oriental tobaccos (IARC V.38, 1986).

REGULATIONS

Applicable regulations are given in detail in the Regulations table. Federal regulations related to tobacco products that concern taxation, customs duties, the potential for hand-to-mouth transfer of toxic substances when using tobacco in the workplace, warnings that smoking will exacerbate noncancer risks of certain drugs, and environmental tobacco smoke are not addressed in this section.

The U.S. Food and Drug Administration (FDA) regulates nicotine-containing cigarettes and smokeless tobacco products as nicotine-delivery medical devices under 21 CFR Part 897 "to reduce the number of children and adolescents who use these products and to reduce the life-threatening consequences associated with tobacco use." Measures to reduce the appeal of and access to cigarettes and smokeless tobacco products include numerous restrictions on advertising, including promotional items and event sponsorship. Tobacco-product-dispensing vending machines and self-service displays are prohibited except in adult establishments that do not allow children on the premises at any time. Retailers must request that persons up to the age of 27 present photographic identification bearing their birth date. Free distribution of tobacco products is prohibited. Each package and advertisement must bear the label "Nicotine-Delivery Device for Persons 18 or Older." Cigarettes may not be sold in packages of fewer than 20.

Analyses of FDA jurisdiction over tobacco products (cigarettes and smokeless tobacco products) have been published in the *Federal Register*, including 60 FR 41453-41787, August 11, 1995, with a correction at 60 FR 65349-65350; 61 FR 44615 ff., August 28, 1996; and 61 FR 45219-45222, August 28, 1996. FDA published Children and Tobacco Executive Summaries (U.S. FDA, 1996 a,b), which are available free on the Internet and by mail.

The Federal Trade Commission (FTC) of the Department of Commerce administers the Federal Cigarette Labeling and Advertising Act, Public Law 89-92 as amended through Public Law 98-474 (15 U.S. 1331) (FTC, 1998). Provisions include the ban of cigarette advertisements on radio and television, submission of annual reports to Congress on current practices and methods of cigarette advertising and promotion and recommendations for appropriate legislation,

and requirement of rotation of four warning statements placed conspicuously on cigarette packages and advertisements. One of the warning statements is "SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy." The last four words may be omitted on billboards.

The Federal Communications Commission (FCC) shares responsibility with FTC for the ban of advertisements of cigarettes and smokeless tobacco on radio and television (FTC, 1998).

The Department of Health and Human Services (DHHS) also has responsibilities under the Federal Cigarette Labeling and Advertising Act, 15 U.S.C. Section 1341, Smoking, Research, Education, and Information. DHHS was given mandates to establish and carry out a program to inform the public of any human health dangers of cigarette smoking. All activities, including educational and research programs within DHHS shall be coordinated with similar activities of other Federal and private agencies via the Interagency Committee on Smoking and Health. DHHS shall collect, analyze, and disseminate information, studies, and other data associated with cigarette smoking that is relevant to human health. DHHS shall develop standards, criteria, and methodologies for improved information programs related to smoking and health. DHHS is to compile State and local laws relating to cigarette use and consumption. From January 1, 1986, and biennially thereafter, the Secretary of HHS shall transmit a report to Congress that contains an overview and assessment of educational efforts by Federal agencies and the extent of public knowledge regarding health consequences of smoking, a description of DHHS and Interagency Committee activities, and a description of private sector activities in response to the effects of smoking and health. Regulations were not identified that corresponded to all of these mandates. However, CDC publications such as the Surgeon General's reports and the National Cancer Institute's monographs in the Smoking and Tobacco Control series appear to fulfill several of these mandates.

The Centers for Disease Control and Prevention's (CDC) Office on Smoking and Health (OSH) is the delegated authority to implement major components of the DHHS's tobacco and health program, which comprises programs of information, education, and research. CDC's authority includes collection of tobacco ingredients information to facilitate HHS's overall goal of reducing death and disability from use of tobacco products (CDC, 1997).

HHS, under 45 CFR Part 96-Subpart L-Substance Abuse Prevention and Treatment Block Grant, requires that to be eligible for Block Grants to support substance abuse prevention and treatment services, each State must have in effect and strictly enforce a law that prohibits sale or distribution of tobacco products to persons under age 18 by manufacturers, distributors, or retailers.

Federal agencies have issued regulations to implement Public Law 104-52, the Prohibition of Cigarette Sales to Minors in Federal Buildings and Lands. The General Services Administration (41 CFR), the Treasury Department (31 CFR), and the Railroad Retirement Board (20 CFR) prohibit the vending and free distribution of tobacco products on property under their jurisdictions.

Under 32 CFR 85.6, health promotion efforts in each military service should include smoking prevention and cessation programs. Health care providers are encouraged to take the opportunity at routine medical and dental examinations to apprise service personnel of tobacco use risks (including smokeless tobacco) and how to get help to quit. Regulations are summarized in Volume II, Table A-42.